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☑	USPT	(L1 and kinase) AnD ((@pd > 20021204)!)	YES	ADJ	ASSIGNEE	L3
☑	USPT	(L3 and Nck) AnD ((@pd > 20021204)!)	YES	ADJ	ASSIGNEE	L4
☑	USPT	p75NTR	YES	ADJ		L5
☑	USPT	NADE	YES	ADJ		L6
☑	USPT	L6 and L5	YES	ADJ		L7
☑	USPT	L6 and bind$3	YES	ADJ		L8
☑	USPT	bex3 or bex-3	YES	ADJ	ASSIGNEE	L9
☑	USPT	NGFR-asoociated protein 1	YES	ADJ	ASSIGNEE	L10

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***300361** Links

NERVE GROWTH FACTOR RECEPTOR-ASSOCIATED PROTEIN 1; NGFRAP1

Alternative titles; symbols

NGFR-ASSOCIATED PROTEIN 1
p75(NTR)-ASSOCIATED CELL DEATH EXECUTOR; NADE

Gene map locus Xq22.1-q23

TEXT

The C-terminal cytoplasmic domain of p75(NTR) (NGFR; 162010) has a type-2 death domain. However, TRAF (e.g., TRAF6; 602355)-like proteins that interact with this domain do not affect NGF (162030)-dependent apoptosis. Using a yeast 2-hybrid screen with the cytosolic domain of p75(NTR) as bait, Mukai et al. (2000) obtained cDNAs encoding mouse and human p75(NTR)-associated cell death executor, or NADE. Human NADE is identical to the HGR74 cDNA cloned by Rapp et al. (1990) from an ovarian granulosa cDNA library. HGR74 was expressed in testis, prostate, seminal vesicle, and ovarian granulosa cells (Rapp et al., 1990). By sequence analysis, Mukai et al. (2000) predicted that the 111-amino acid NADE protein has a leucine-rich nuclear export signal (NES) and 2 ubiquitination sequence boxes. Western blot analysis showed expression of mouse Nade only after proteasome inhibition, implying that native Nade is modified by the ubiquitin conjugating system. Immunofluorescence microscopy demonstrated expression of wildtype Nade, but not Nade carrying leu94-to-ala and leu97-to-ala mutations in the NES, in the cytoplasm. GST pull-down analysis indicated that the C terminus of Nade binds to the cytoplasmic cell death domain of p75(NTR). Coimmunoprecipitation analysis showed that NGF induces interaction of NADE and p75(NTR). Tunel analysis determined that NGF, but not other neurotrophins, could induce apoptosis in cells expressing NADE and p75 (NTR). NGF-treated cells expressing NADE and p75(NTR) processed CASP2 (600639) and CASP3 (600636) to their active forms. Confocal microscopy established that most NGF-treated oligodendrocytes underwent apoptosis and expressed NADE.

Scott (2001) mapped the NGFRAP1 gene to Xq22.1-q23 based on sequence similarity between the NGFRAP1 sequence and the chromosome X clone RP13-349O20 (GenBank AL606763).

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Personal Communication. Baltimore, Md., 10/8/2001.

CONTRIBUTORS

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CREATION DATE

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EDIT HISTORY

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L5: Entry 1 of 5 File: USPT May 6, 2003

US-PAT-NO: 6558912
DOCUMENT-IDENTIFIER: US 6558912 B1

TITLE: NRAGE nucleic acids and polypeptides and uses thereof

DATE-ISSUED: May 6, 2003

INVENTOR-INFORMATION:

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Salehi; Amir	Point Claire			CA

US-CL-CURRENT: 435/7.23; 435/7.1, 435/7.21

CLAIMS:

What is claimed is:

1. A method for identifying a compound that modulates apoptosis, said method comprising: (a) contacting (i) a p75NTR polypeptide; (ii) an NRAGE polypeptide comprising at least 90% sequence identity to SEQ ID NO: 1 or SEQ ID NO: 2, said NRAGE polypeptide capable of binding said p75NTR polypeptide; and (iii) a candidate compound; and (b) monitoring the level of binding of said NRAGE polypeptide to said p75NTR polypeptide, wherein a change in said level of binding in the presence of said candidate compound, relative to a level of binding of said NRAGE polypeptide to said p75NTR polypeptide in the absence of said candidate compound, identifies said candidate compound as a compound that modulates apoptosis.

2. The method of claim 1, wherein said contacting takes place in a cell.

3. The method of claim 1, wherein said cell is in a mammal.

4. The method of claim 1, wherein said cell is from a mammal.

5. The method of claim 4, wherein said mammal is a human or a rodent.

6. The method of claim 1, wherein said contacting takes place in a cell-free system.

7. The method of claim 1, wherein said NRAGE polypeptide is human NRAGE (SEQ ID NO: 1) or rat NRAGE (SEQ ID NO: 2).

8. The method of claim 6, wherein said NRAGE polypeptide is human NRAGE (SEQ ID NO: 1) or rat NRAGE (SEQ ID NO: 2).

9. The method of claim 2, wherein said cell is in vitro.

10. The method of claim 9, wherein said NRAGE polypeptide is human NRAGE (SEQ ID NO: 1) or rat NRAGE (SEQ ID NO: 2).